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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re: Patent Application of Harry R. Davis : PATENT APPLICATION
Serial No.: 10/057,534 : Group Art Unit: 1617
Filed: January 25, 2002 : Examiner: Shengjun Wang
For: Combinations of Bile Acid Sequestrant(s) and Sterol Absorption Inhibitor(s) and :
Treatments for Vascular Indications : Atty. Docket No.: CV01378K

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

REQUEST FOR RECONSIDERATION

This Request for Reconsideration is being submitted in response to the Office Action mailed on October 16, 2003 (Paper No. 9).

Applicant herewith petitions the Commissioner of Patents and Trademarks to extend the time to reply to the Office Action dated October 16, 2003 for one month from January 16, 2003 to February 16, 2004 and attached hereto is a Petition for Extension of Time authorizing payment of the extension fee from Deposit Account No. 19-0365. Since the February 16, 2004 is a federal holiday, this response is being timely filed on February 17, 2004.

Claims 1-3, 5-28, 31-36, 70-72, 74-77, 79 and 80 are pending in the application. Claims 4, 29, 30, 37-69, 73, 78 and 81 have been withdrawn from consideration by the Examiner as being non-elected.

At pages 3-4 of the Office Action, claims 1-3, 5-28, 31-36, 70-72, 74-77, 79 and 80 have been rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 5,631,365 ("Rosenblum et al.") in view of U.S. Patent No. 5,300,288 ("Albright"), U.S. Patent No. 4,837,255 ("Dechow") and U.S. Patent No. 5,661,145 ("Davis").

For brevity, the reasons for rejection are not repeated herein but reference is made to the outstanding Office Action.

Applicant respectfully traverses this rejection and requests that the rejection be reconsidered and withdrawn.

It is respectfully submitted that the combination of the references cited by the Examiner as rendering the claimed invention obvious is improper because there is no suggestion in the cited references to combine the claimed components of ezetimibe and cholestyramine.

The law is replete with cases holding that there must be some suggestion or motivation in the prior art to combine the references. When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

In the Kerkoven case cited by the Examiner, the Court found the motivation or suggestion to combine two materials each disclosed in a separate reference from the fact that each reference taught the individual materials for the very same purpose as in the claimed combination. That is not the situation here.

Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. See ZETIA™ (ezetimibe) Tablets Package Insert at column 1 (Merck/Schering-Plough Pharmaceuticals) (October 2002) included in the Information Disclosure Statement filed January 15, 2004 (copy attached for the Examiner's convenience as Exhibit A).

The cholesterol content of the liver is derived predominantly from three sources. Id. The liver can synthesize cholesterol, take up cholesterol from the blood from circulating lipoproteins, or take up cholesterol absorbed by the small intestine. Id. Intestinal cholesterol is derived primarily from cholesterol secreted in the bile and from dietary cholesterol. Id.

Ezetimibe has a mechanism of action that differs from those of other classes of cholesterol-reducing compounds (HMG CoA reductase inhibitors, bile acid sequestrants (resins), fibric acid derivatives, and plant stanols). Id.

Ezetimibe does not inhibit cholesterol synthesis in the liver (like HMG CoA reductase inhibitors), or increase bile acid excretion (like bile acid sequestrants). Id. Instead, ezetimibe localizes and appears to act at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. Id. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood; this distinct mechanism is complementary to that of HMG CoA reductase inhibitors. Id.

Ezetimibe does not operate by the same mechanism as either cholestyramine or cholesterol biosynthesis inhibitors. Because of the difference of the way that each component of the presently claimed combination acts, it is respectfully submitted that the rejection is based upon an improper combination of references. There is no suggestion or motivation in the references to combine the claimed components that operate by these different mechanisms.

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Accordingly, reconsideration and withdrawal of the §103(a) rejection is respectfully requested.

Applicant respectfully requests that the Examiner return an initialed PTO-1449 form for each of the Information Disclosure Statements submitted on August 21, 2002 (EFS Nos. 17231 and 17260), April 4, 2003, October 30, 2003, November 26, 2003 and January 15, 2004, indicating that the Examiner has considered each of the references cited therein.

In view of the foregoing remarks, it is respectfully submitted that all of the pending claims in the present application are distinguishable from the cited prior art. Accordingly, reconsideration and withdrawal of the rejection and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

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Date: February 17, 2004


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